Connective Tissue Diseases

= diseases of Dermis

(1) Lupus erythematosus (LE)

(Zeba hamra)

Chronic discoid EL	Subacute cutaneous LE	A systemic LE	Mixed C.T diseases	Drug induced LE
• Skin lesions +ve. • Systemic lesions : -ve • Serology : -ve the AN A in few PT's • HLA B7 & B8	• Skin lesions : ± • Systemic lesions : ± (muscle joint) • Serology : +ve Anti-Ro & Anti-La • HLA-DR3 & B8	• Skin lesions : +ve • Systemic lesions : ++ve • Serology : +ve ANA +ve and antismith • No HLA association		+ve antihistone Ab

[I] Chronic Cutaneous Lupus Erythematosus (Discoid LE)

Red + DLE well defined scarring discoid plaques

* **Epidemiology** :

- Age : 40-80 years old.
- Sex : female : male = 2 : 1 (more sever in blocks)
- ↑ incidence of HLAB7 & B8

* **Clinically** :

precipitating factor

- PPF : infection, stress, sunburn & drugs e.g. griseofulvin.

  N.B. : "It may start spontaneously"

- Exacerbating factors : sunlight.
- Symptoms : Disfiguring erythematous scaly lesions mostly in the face.

* healing → thin white atrophic non contractile scar

Causes of ulcer in DLE:-

- Iatrogenic
- systemic
- ulcerative type.

+ ANA ⟶ elderly
weak in DLE
pregnancy
malignancy

Types of scales in Derma

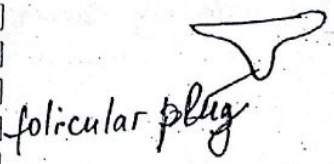
Myca scale ⟶ Pityriasis Lichenoid Chronica
adherent " ⟶ DLE
Laminatted ⟶ Ps
Cigeratte paper ⟶ T versicolour
Collaratte ⟶ P. Rosea.

- Signs :

> Sites lesions usually affect the sun exposed areas i.e. : Face (specially the checks & bridge of nose {butterfly area} ears & V-shaped area of the chest.

> Lesions are in the form of well defined erythematous plaques with variable shape & size having an elevated border. The border of the plaque adjacent to the skin is some times telangectatic.

> The surface of the plaques is covered with small grayish adherent scales which when removed, their under-surface show horny plug. This horny plug has occupied a dilated pilosebaceous canal (follicular plugging). The follicles become dilated & prominent giving what is called stippling sign. The center of the lesion is usually depressed.



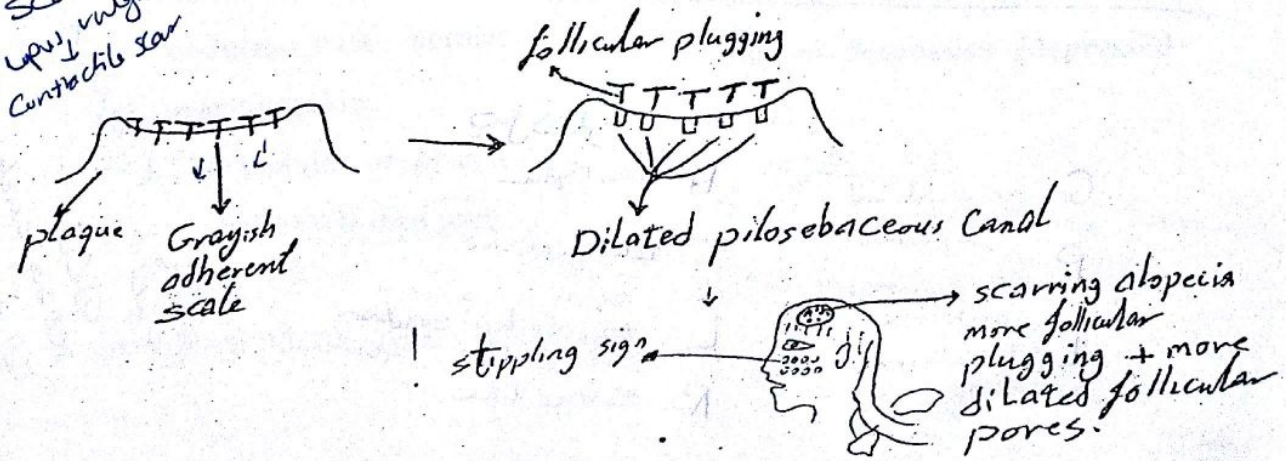
wide follicular pores

> The lesions tend to heal with scarring, atrophy & pigmentary changes. (no treatment → skin cancer)

> On the scalp the plaques show more infiltration & more scar formation. Plugging & dilatation of the follicles are more pronounced. Loss of hair is permenant (cicatricial alopecia).

healed with thin white non-atrophic non-contractile scar

D.D lupus vulgaris contractile scar



clinical varian

① Localized.
② generalized.
③ hyperthophic.
④ papular DLE → pruritic papule on the back → resulting in acneform hyperthophic follicular scar.

⑤ Roseacea like DLE → diffuse erythema reddish nodules (but not pustules) on cheeks, nose, forhead, chin.

⑥ palmoplanter erosive DLE.

⑦ annular atrophic DLE.

⑧ Telangectatic DLE → persistent reticulate telangectasia Face / ear / neck / dorsa of hands.

⑨ LE gyratum repens :- migratory gyrate annular erythema + histological feature of DLE + underlying carcinoma

~~⑩ lupus profundus~~.

other clinical types of DLE :- ① classical.

② LE Tumidus	Lupus panniculitis	chillblain lupus
ion :- erythema, induration . heal without scarring . No scales . No follicular - plugging. . Common on face . very low prevelance SLE DIF → Non specific. H/P → normal epi dermal inf. infiltrate ē marked mucin deposition	intense inflamation of sc fat - firm nodules or plaque sharply defined ē normal overlying skin better felt than seen . healing with cupshaped depression. . some patient, have discoid lesion overlying the panniculitis Face, upper trunk, upper arm, Breast Buttock, thigh	. Red or dusky papule. papule or nodule. . on toes, fingers, nose knee, elbow . DLE present elsewhere - Caused and excerbated by cold or pregnancy.

جيل هتلر

G generalized
P papular / palmoplanter / profundus
L localized

H hypertrophic
T telangectatic
L LP over lap syndrom / LE gyratum repens
R Roseace like

perni...
① LE
② sarcoidosis
③ perniosis

mucous membrane affection (3%), Nail affection, eye affection, ectropion, Conj. redness

N.B. :

→ Active DLE lesions are bright red, while on healing lesions may show pink or white (hypomelonaotic) macules & scars. Lesions may show hyperpigmentation especially in persons with brown or black skin.

atrophic non contractile

→ 5% of cases of DLE change into SLE.

→ Neoplastic changes e.g. SCC or BCC occur on top of DLE. They are often aggressive.

Clinical Types :

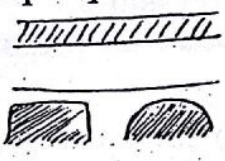
1- Localized DLE. Lesions are localized above the neck.

2- Generalized (Disseminated) DLE. Lesions are above & below the neck.

3- Hypertrophic (verrucus DLE) :

- Non pruritic papulonodular lesions simulating hypertrophic LP or keratoacanthoma.
- Treatment : Intralesionsl steroid.

4- Lupus profundus (lupus panniculitis) : in subcutaneous tissue



- **Firm S.C plaques or nodules with normal overlying skin.** → **Healing occur with cup-shaped depression (depressed scar)**
- **The nodules or plaque are better felt than seen**

atrophy → Cavities hypopigmented or depigmented

5- LE-lichen planus overlap syndrome.

D.D. Causes of pigmentary incontinence:-

① LP ② LE
③ LSA ④ FDE
⑤ Dermatomyositis.
⑥ incontinentia pigmenti

D.D. of Colloid bodies < LE / LP

Colloid bodies

- Civatte bodies in Lichenoid tissue eruption
- Large apoptotic keratinocytes
- present as round or ovoid homogenous eosinophilic str
- seen in dermatosis é degenerated keratinocytes
  → "interface dermatitis"

as:- LP, FDE, GVHD, poikiloderma., DLE

* Diagnosis :

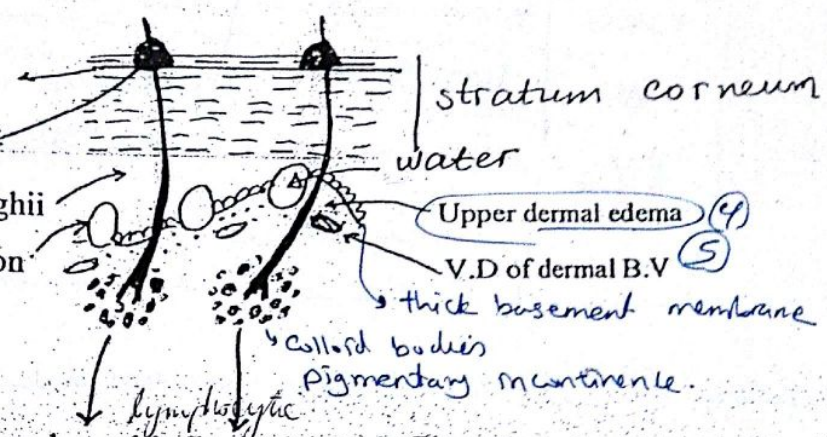
1. History & clinical examination.

2. Histopathology :

(1) Hyperkeratosis with follicular plugging.

(2) - Atrophy of st. Malpighii

(3) - Hydropic degeneration of basal cell layer.



Diagnostic → (6) Patchy peri appendageal inflammatory infiltrate.

DD of patchy dermal infiltrate

1. LE. (SL)
2. Polymorphic light eruption.
3. Lymphocytoma cutis.
4. Lymphocytic infiltration of the skin (Jessner's)
5. Lymphocytic lymphoma.

Hydropic degeneration of basal cells :

1. LE. 2. LP. (3L)
3. Dermatomyocitis. 4. Lichen sclerosis et atrophicus

3. Immunofluorescence (lupus band test).

DIF : granular deposits of IgG at the dermo-epidermal junction (In 75% of active lesions)

4. Other lab examination :

- ↑ ESR.
- ↑ leucopenia.
- +ve ANA in very few patients. — ve serology

Q Systemic therapy for DLE:.

① Systemic antimalarial therapy (Gold standard):-

	Hydroxy-chloroquine	chloroquine	Quinacrine
safety	most safe	most toxic	
Dose	200-400 mg/d	125-250 mg/d	100 mg/d
eye	less toxic	more toxic	Not toxic turn skin yellow
max. dose	6.5 mg/kg . Bw. most common used	3.5 mg/kg B.w	used in resistance to Hydroxy chloro

② Systemic therapy for antimalarial.-

- Dapsone 100mg/d. For bullous emption
- Retinoid
- thalidomide
- steroid

- **Differential diagnosis.**
  - Actinic keratosis.
  - Seborrhic dermatitis.
  - Plaque psoriasis.
  - Polymorphic light eruption.
  - Lichen planus.
  - Lupus vulgaris. → scaring disease

- **Treatment :**

① Topical
- Avoid sunlight.
- Topical sunscreen. spf 15
- Topical steroid.
- Intralesional injection of steroid → (hypertrophic DLE)
- Systemic treatment :
  - Antimalarial : (Plaquenil)
    - Dose : 200-400mg/day.
    - Ophtholmogenic monitoring every 4-6w.
  - Systemic steroid for widespread or disfiguring lesions (should be limited to 4-6 weeks).
  - Systemic etretinate 1mg/kgm BW may be indicated in hyperkeratotic DLE.

④ Topical calcineurin inhibitor
⑤ Topical retinoids.

Anti-malarial = Immunosuppressive action

(Skin pigmentation)

☆ Stop smoking

In case of failure of steroid/antimalarial therapy the following can be tried :

- Clofazamine (lamprene) 100-300mg/d.
- Vit. E 600IU/d.
- Dapsone 100mg/d (usually for bullous lesions).
- Thalidomide : highly effective but teratogenic & neurotoxic.

Powel's Syndrome :-
Erythema multiforme like + Cut. LE

Diagnosis :- clinical → minor criters
major criter

presence of LE (DLE, SCLE, SLE)
LE- like lesion
Speckled pattern of ANA

- anti Lo anti Ro
- RF

3 major + 1 minor

Site :- Face. Neck. Chest

D.D → EM → precipitated by HSV ؟ -ve RF ؟ -ve ANA ؟ HH by Cs ؟ HH of cause

HIE → dermal edema, Keratinocyte Necrosis

DIF → at DEJ IgG, C3

★ Chillblain → do serology to exclude LE

★ variety of DLE
↓
pre-ve serology

- Monoclonal CD4 antibodies is to be considered as a noval treatment for sever cutaneous LE.

Course & Prognosis :

1. 5% of cases may develop systemic LE.
2. 50% of cases with localized lesions → complete remission.
3. 10% of cases with generalized lesions → complete remission.
4. SCC & less commonly BCC → occur in the healed scar of DLE. (untreated lesion)

N.B. :

Chilblain LE :

- Is a chronic unremitting form of LE with acral distribution i.e. : fingertip, rim of ears & heels, especially in women.
- It is usually preceded by DLE on the face.
- Pathogenesis : cold injury to the microvasculature.
- Treatment :
  - Pentoxyphellyn. (red blood cell movement activator)
  - The usual LE treatments are ineffective.

Trental

.acral
.♀
.after DLE
.cold
.Trental

Photosensitive varieties of SCLE — neonatal LE, anti c..

[II] Subacute Cutaneous LE (SCLE)

* **Epidemiology** :

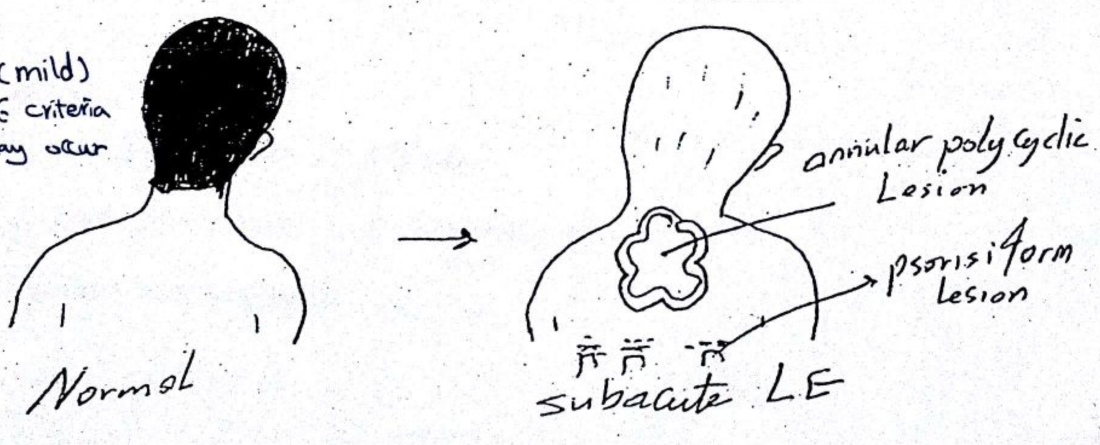
- Age : Young or middle aged.
- Sex : female : male = 2 : 1.
- ↑ Incidence of HLAB8 – DR3.

* **Clinically** :

- ***Exacerbating factors*** : Sunlight.
- ***Symptoms*** :
  - ➔ Sudden onset of disfiguring erythematous eruption appearing on the upper trunk & dorsa of the hands.
  - ➔ +ve constitutional symptoms e.g. malaise …
  - ➔ Photosensetivity.
- ***Signs*** :
  - ➔ Sites : Lesions usually affect the back, front of the trunk, around the neck, the arms (face is rarely affected).
  - ➔ Lesions are in the form of non-scarring psoriasiform papulosquamous (in 2/3 of cases) or annular polycyclic (in 1/3 of cases).
  - ➔ There is no scar or atrophy. — healed with greyish white hypopigmentation
  - ➔ Diffuse non scarring alopecia can be found.

DLE → scarring
SCLE → Not

* Systemic lesion (mild)
- 50% Fullfil SLE criteria
- Lung disease may occur
- Renal — rare

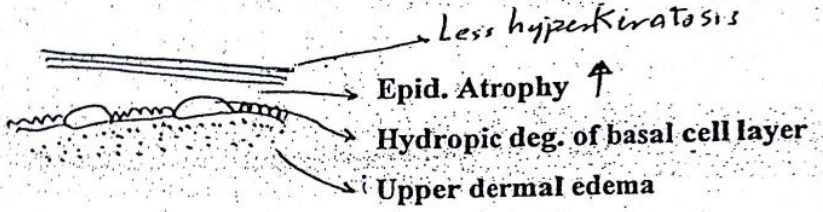


- ***Diagnosis*** :

➔ History & clinical examinations.

➔ Histopathology :

As DLE + more epidermal atrophy & less hyperkeratosis + prominent dermal edema & hydropic degeneration of basal cell layer.



➔ Immunofluorescence : Lupus band test

DIF : +ve in 40% of cases.

➔ Serological findings :

⇨ Low titers of ANA (homogenous pattern).

⇨ High levels of circulating immune complexes.

⇨ Antibodies to RO/SS-A antigen are present in more than 60% & LA/SS-B much less commonly.

anti-Ro +ve
anti-La +ve
↓ ANA

Anti cytoplasmic Ab
Anti nuclear Ab
IgG
(cytoplasm)
FANA → homogenous type in 60% patient

N.B. :

The extensive involvement is more seen in patient with chronic DLE.

Treatment :

1. Avoid exposure to heat & sun.
2. Avoid certain drugs e.g. Grisofulvin.
3. Topical corticosteroid.

4.. Systemic therapy (the main-line of treatment)

a. Hydroxychloraquine 400mg/d for 4-8weeks.

b. If the above faild retnoids (acitretin) may be tried.

c. Thalidomide (200-300mg/d) : very effective for skin lesions (but not for systemic involvement.

d. Dapsone & cyclosporm have been tried with varing results.

Prognosis & Course :

Very good, the skin lesions can completely disappear.

[III] Systemic LE

It is a serious multisystem disease involves the connective tissue & blood vessels.

* **Epidemiology** :

→ Age : 30y in female and around 40y in male.

→ Sex : female : male = 8: 1 (more sever in black).

→ Family history +ve in 5% of cases.

* **Etiology** :

→ Genetic : more in pt with HLAB8 & DR3.

→ Heredity

→ Drugs :

⇨ Flare up can be induced by contraceptive pills & hormone replacement therapy.

⇨ Hydralazine, anticonvulsants & methyldopa.

→ Viral agent.

→ Immunologic abnormalities : (there is loss of self tolerance)

⇨ B cell activation result in → hyper-gamaglobulinaemia.

→ UV radiation → important role in initiation disease. (↑ cytokines, chemokines → ↑ immune resp.)

immunological → loss of self tolerance → B cell activation → ↑ Ig

⇨ Development of immune complexes from the circulation leads to → deposition of complexes in the tissue. Causing → vasculitis in different organs e.g. glomerulonephritis.

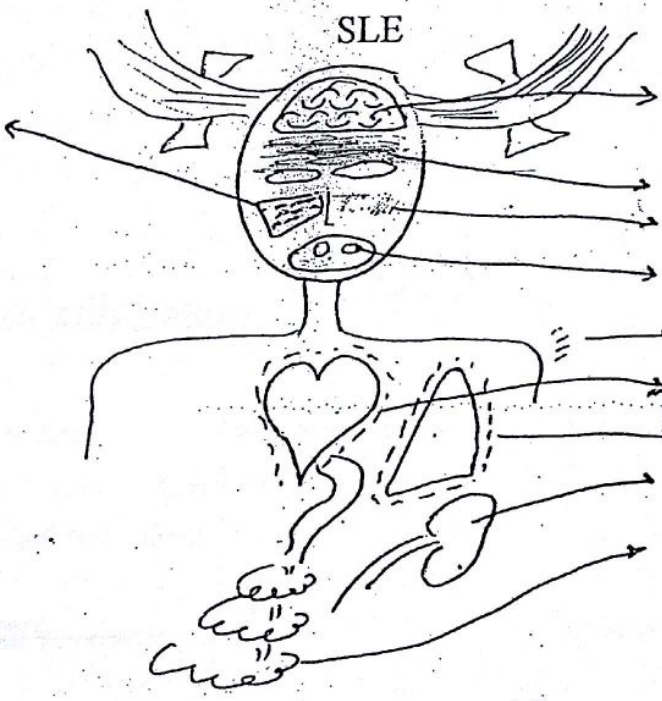
* **Clinically**:

→ SLE is very variable in its manifestation.

→ Mild cases may present only with arthralgia while sever cases man present with multisystem involvement.

→ The duration of lesions is weeks (acute) or months.

* The American Rheumatism Association Criteria for diagnosis of SLE



(1) Neurologial disorder e.g. psychosis

(2) Photosensetivity.

(3) Malar rash.

(4) DLE lesion

(5) Oral ulcers

(6) Arthritis.

(7) Pericarditis

(8) Pleuritis

(9) Renal disorders

(10) Haematological disorder e.g. Haemolytic anemia, leukemia & thrombocytopenia.

(11) Immunological abnormalities e.g. +ve LE cell.

(12) +ve antinuclear antibodies.

(short cut hair, scalp free)

- discoid rash
- lupus hair
- palmar erythema
- livedo reticularis
- erythema nodosum

The presence of 4 or more of these criteria → diagnostic.

MD SOAP BRAIN

M → malar rash
D → Discoid LE

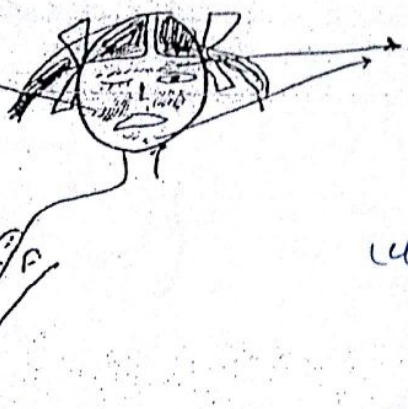
S → serositis ← pleuritis, pericarditis
O → oral ulcer
A → arthritis
P → photosensitivity

B → haematological
R → Renal
A → ANA
I → immunological → anti ds DNA, anti sm, LE test
N → neuropathy, psychosis

Cutaneous manifestations of SLE (+ve in 75% of cases)

(I) Spesific lesions (diagnostic) :

(1) Malar rash heal without scar
- on malar prominence
- Spare naso labial fold



(2) Photosensetivity : dermatitis in exposed areas.

(3) Bullus lesions : due to separation at DEJ (may be due to antibodies to type VII antigen) best treated by dapsone (MCQ)
Clinical → as BP, EBA
HIP → as OH, BP, EBA
② → bullous crusted lesion as a result of intense basal cell damage
③ dramatic acute eruption as TEN may occur

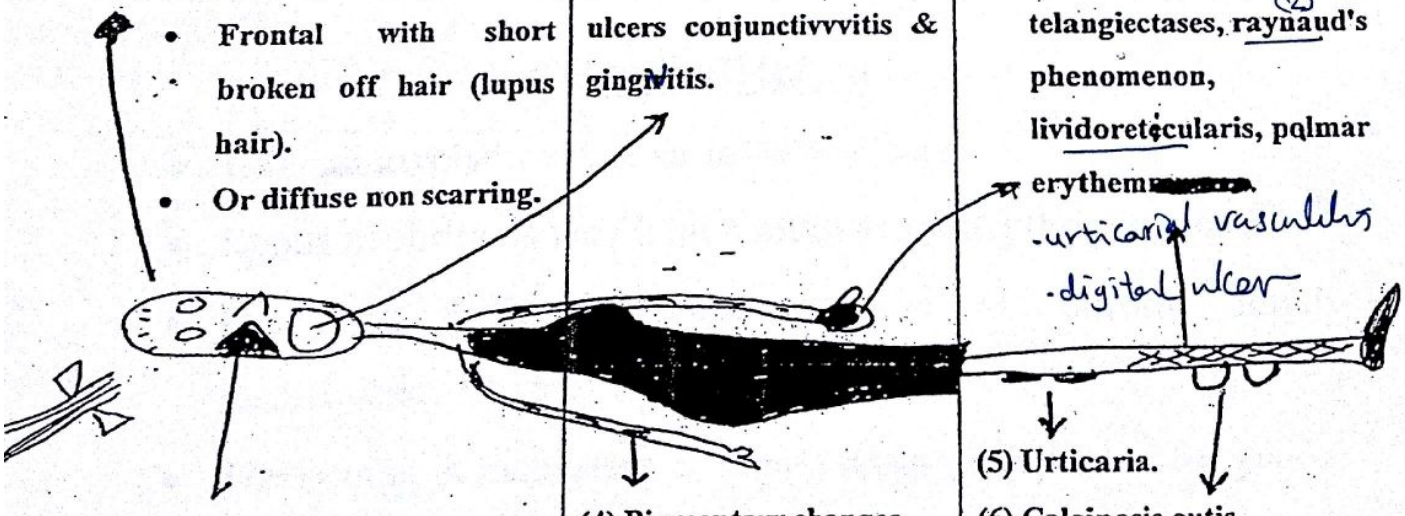
(4) wide spread erythema on V shaped chest
shoulder
extensor of arm
back of hand

(II) Non specific lesions :

(1) Alopecia : (40-60%)
- Frontal with short broken off hair (lupus hair).
- Or diffuse non scarring.

(2) MM lesions erosion & ulcers conjunctivvvitis & gingivitis.

(3) Vascular lesions periungual telangiectases, raynaud's phenomenon, lividoreticularis, palmar erythema
- urticarial vasculitis
- digital ulcer



Discoid rash

(4) Pigmentary changes

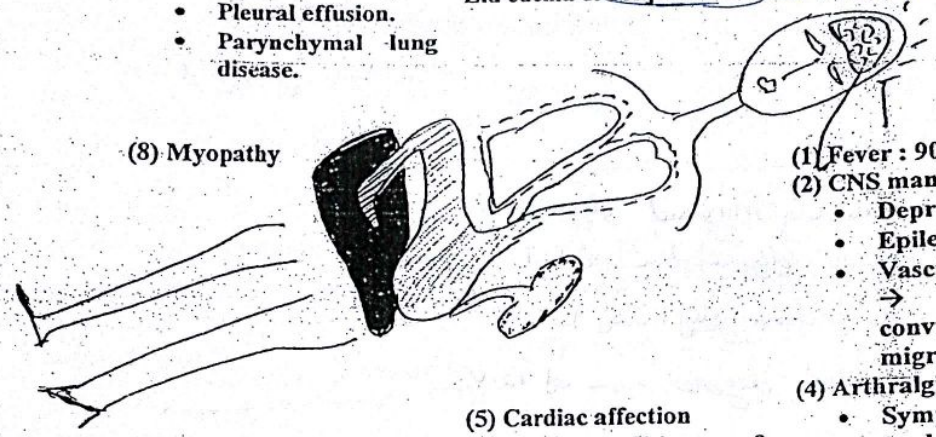
(5) Urticaria.

(6) Calcinosis cutis

Systemic manifistations of SLE :

(9) Lung affection :
- Pleuritis.
- Pleural effusion.
- Parynchymal lung disease.

(3) Eyes :
* Retinal vasculitis. → retinal hge
Lid edema & conjunctivitis. → in old patient, true anti Ro



(8) Myopathy

(1) Fever : 90% of cases.
(2) CNS manifestations :
- Depression.
- Epilepsy.
- Vasculaitis of CNS → hemiplegia, convulsions & migrane ...

(4) Arthralgia : 90%
- Symptoms similar to rharthritis.
- Small joints commonly affected.
- Deformities uncommonly affected.
- Deformities uncommonly occur.

(5) Cardiac affection
- Pericarditis & pericardial effusion
- Myocarditis.
- Endocarditis.

(6) GIT affection
- Nausea vomiting & diarrhea.
- Oesophegeal dysmatility.
- Ulcerative colitis.

Renal affection

- Clinical involvement occur in 40% of cases.
- Lupus nephritis is very important in assessing the prognosis.
- Focal or diffuse glomerulonephritis → chronic renal insufficiency → renal failure.
- The course is inconstant & albuminuria may persist for years without marked deterioration in renal function.

Associations :

- Rh arthritis, Hashimoto's thyroiditis, sjögren's syndrome & Dermatomyositis.

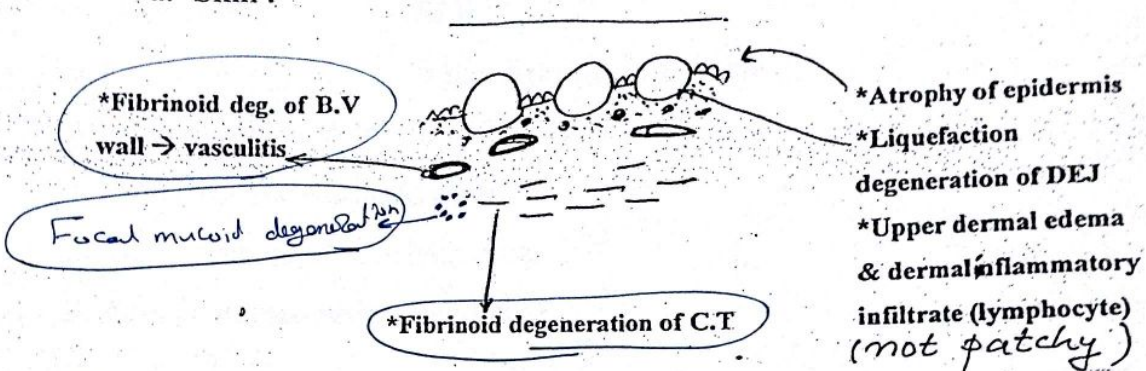
SLE
- Focal mucoid degeneration.
- Fibrin degeneration of CT
- Liquefaction deg. of DEG
- Fibrinoid degeneration of B.V.

Drug-induced lupus syndrome :

- Hydralazine – Isoniazid – D-pencillamine (to memorize them)
  (no cutaneous manifestations)

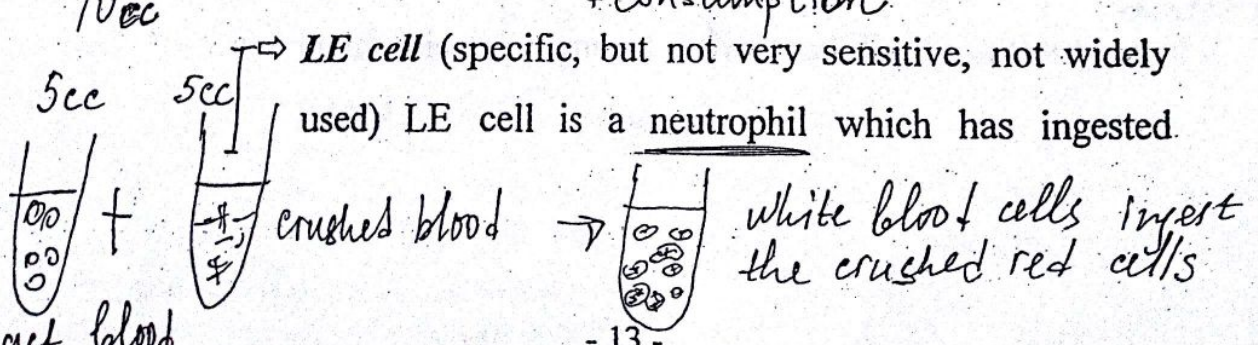
Diagnosis :

1. History & clinical examination
2. *Histopathology* :
   a. Skin :



!!! b. Other organs : Widespread vasculitis affecting capillaries, arterioles & venules → necrosis → systemic organ failure

3. *Lab. Investigations* :
   - ⇨ ***Urine*** : proteinuria (> 3.5gm/d) cellular cast & RBCs.
   - ⇨ ***Blood*** : pancytopenia.
   - ⇨ ***ESR*** : raised. (every month)
   - ⇨ ***Wasserman reaction*** : +ve (nonspesific Ab)
   - ⇨ ***Hypergammaglobulinemia***: Rh. factor is +ve in 30-50% of patients.
   - ⇨ ***Serum complement*** : levels are reduced during active disease. (due to multisystem vasculitis & consumption)
   - ⇨ ***LE cell*** (specific, but not very sensitive, not widely used) LE cell is a neutrophil which has ingested



basophilic homogenous nuclear material from another leucocyte in the presence of LE factor.

⇨ ***Direct IF test (lupus band test)*** :

- Detection of IgG & complement at DEJ (in sublamina densa).
- It is used to differentiate between DLE & SLE.
- It has a prognostic value.

The test depends on detection of IgG & C in 3 areas :

1. Sun exposed diseased area.
2. Sun exposed uninvolved area.
3. Sun protected uninvolved area.

	DLE	SLE
(1) Sun exposed involved area.	**+ve 90% cases**	**+ve in 90% of cases**
(2) Sun exposed uninvolved area.	**-ve**	**+ve in 78% of cases**
(3) Sun protected uninvolved area	**-ve**	**+ve in 55% of cases → indicate renal affection**

⇨ ***Indirect If Test (FANA test)*** : (blood)

- +ve in 80% of cases.
- Using mouse liver as a substrate, 4 staining patterns can be demonstrated. + patients blood + fluorescent material
- Diagnosis & prognosis differ accordingly to the type of FANA.

FANA	Antibody	Diagnosis	Prognosis
1) Peripheral 	n DNA →	SLE (specific) →	Poor
2) Homogenous 	n DNA →	SLE →	Poor
	Nucleohistone →	SLE (drug induced) →	Good
		مثل SCLG	
3) Nucleolar 	nuclear RNA	SLG Systemic scleroderma	poor
5) Centromere	kinetochore	CREST	Good
4) Speckled  like broken glass.	Sm →	SLE(specific) →	Poor
	RNP' →	Mixed connective tissue disease →	Good

⇨ ***Serological markers*** : (circulating Ab against Ag in nucleus and cytoplasm)

[I] Antibodies against nuclear constituents :

1) *Anti DNA antibodies* :

- Native DNA Abs = double stranded DNA Abs : (very 6 months)
  - Highly specific for SLE.
  - Present in 70-75% of pt with active SLE associated with nephritis.
  - Measured by RAI, ELISA or IIF.
- Single stranded DNA Abs :
  - Present in 90% of SLE pt.
  - Non specific (+ve in other C.T. diseases & occasionally in DLE).

Q Drug-induced LG:-

- hydralazine, procainamide, Isoniazid:-
  - produce LG like C/P
  - rare cut, Renal symptoms.
  - -ve anti dsDNA
  - +ve ANA, +ve Anti histone.
  - improve ē drug withdrawal

- D-penicillamine → differ in
  - Frequent cut, Renal C/P
  - +ve anti dsDNA

- Hydrochlorothiazides → SCLE-like lesion
  → +ve anti Ro

- Biologic inhibitor → +ve ANA, +ve anti dsDNA
  No LE picture
  -ve anti histone
  DLE, SCLE, photosensitivity → prominent

	Drug induced SLE	Drug induced SCLE
Skin lesion	rare	SCLE or gyrate erythema
Sensitivity	Common	occasionaly
Serology	anti-histone abs	anti Ro
Drugs	- hydralazine - D-penicillamine - minocycline - PUVA	- thiazide - NSAIDs - antihistamine

2) *Antibodies against small nuclear ribonuclear protein (SnRnP)* :

- Anti-Sm antibody :
  - Highly specific for SLE, but occur only in 25% of patients.
  - Associated with high incidence of renal or CNS affection.
- Anti-nRNP (nuclear ribonucleoprotein) Abs +ve in mixed C.T disease.
- Anti La (SS-B) : +ve in 10% of patients with SLE

3) *Histone antibodies* :

- +ve in 30% of SLE.
- +ve in 90% of patients with drug induced SLE e.g hydrolazine or isoniazide.
- C.P : rare cutaneous & renal manifestation.
- Serologically : anti DNA abs are absent.

N.B. : D. penicillamine – induced SLE differ in :

1. Frequent cutaneous & renal manifestations.
2. +ve anti nDNA abs.

[III] Anticytoplasmic Antibodies :

- Small cytoplasmic ribonuclear protein (SC RnP) = Ro.
- Anti Ro abs is +ve in 25% of SLE pt's
- Anti Ro abs is also +ve in :

ANA –ve SLE

- rare
- present é SCLE photosensitivity anti Ro

anti Ro abs true in

- SCLE
- Neonatal LE
- Late-onset LE
- ANA-ve SLE
- Sjogren syndrome

ANA ⟶ more specific in SLE

anti dsDNA ⟶ specific, lipus nephritis ↓monitor activity of nephritis)

anti-Sm ⟶ highly diagnostic, unique

anti-RNP ⟶ behaviour disturbance

anti Ro ⟶ SCLE, NLE

anti La ⟶ usually é anti-Ro

RF ⟶ Not-specific.

Drug induced LE ⟶ according to drug.

anti Ro ⟶ hydrochlorothiazide

anti dsDNA ⟶ biological

anti histone ⟶ hydralazine, INH

ANA

-ve
exclude SLE
good-ve test

+ve
↓
No specific test
anti dsDNA
anti smDNA

ANA +ve in

- healthy
- Pregnancy
- elderly
- autoimmune, SS DM
- Drugs
- infection
- neoplasm

Anti Ro Ab

To memorize

- Subacute cutaneous LE , Neonatal LE, (40 days
  C2 deficiency LE, sjogren's syndrome,
  late onset LE & ANA –ve SLE

⇨ ***Other investigation*** :

Brain CT or MRI

Treatment of SLE :

1. General measures : Rest & avoid sun exposure.
2. NSAI.
3. Prednisone 60mg/d in the following cases ~1-2 tab/daily 60-120mg
   a. CNS involvement
   b. Renal involvement.
   c. Severly ill patients.
   d. Heomolytic crisis.
4. Immunosuppressive drugs (Azothroprine or cyclophosphamide). Imuran.
5. Antimalarial (chloroquine sulphate).
6. Lupus nephritis :
   a. Higher doses of steroid + cyclophosphamide.
   b. Renal dialysis.
7. Raynoud's phenomenon :
   a. Vasodilators.
   b. Avoid smoking & cold.
8. Plasmopheresis.

cytotoxic immunosupression

SLE with Pregnancy

1. Deterioration of renal function occur in 10% of patients. ↑ lupus nephritis
2. Increase risk of premature delivery & perinatal motality.
3. Risk is higher in female patients with +ve anti Ro abs or lupus anticoagulant abs.

- pregnancy has no effect on SLE
- therapeutic abortion not indicated.
- ↑ risk of IUFD in patient ē +ve anticardiolipin Ab

➤ ***Contraception*** :

- Avoid contraceptive pills (aggreivate the disease).
- IUD : high risk of hge & infection.
- Barrier methods one safest for patients.

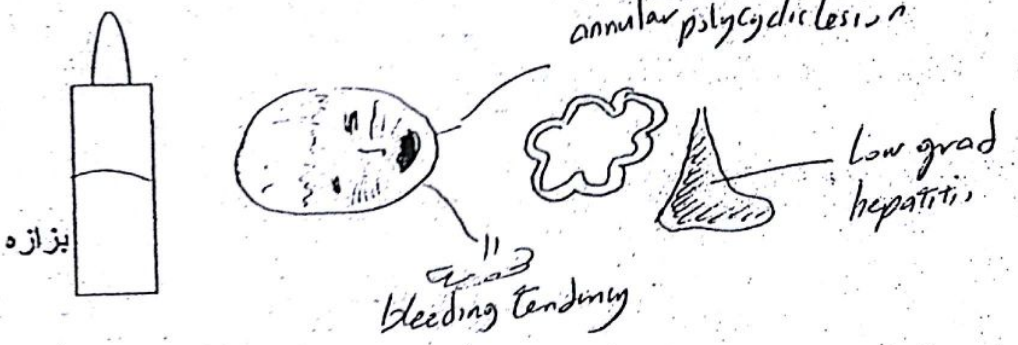
➤ ***Treatment*** :

- Systemic steroid.
- Asprin in low doses e.g. history of thrombosis.
- Closer fetal flow up.

Neonatal LE → type of SCLE

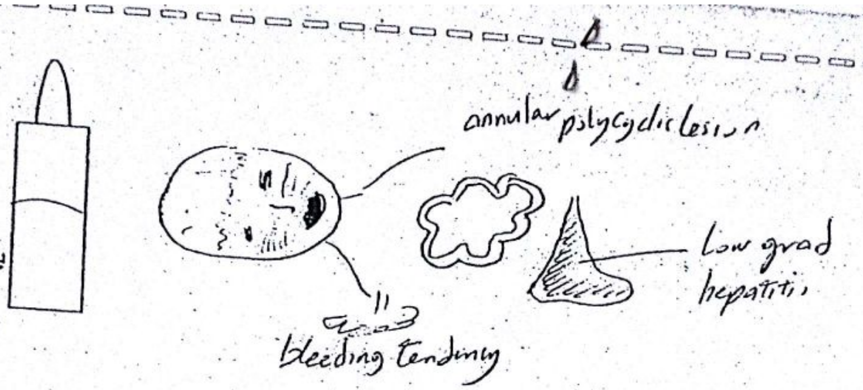
- Female infants of mother who have or will develop C.T disease. → ↑ prevelance of HLA B8, DR3 of mother.
- The infant develop :
  - Subacute CLE – like lesions (annular polycyclic scaly erythematous lesions) mainly on the head & neck. It develop within the first few weeks of life & improve spontinously in 4-6 months, healing with no scarring.
  - Photosensetivity can be prominent.
  - Transient thrombocytopenia & low grade hepatitis.
  - +ve Anti ro-abs in infant & the mother → disappear by 6 months of infant age

site: ① Face → periorbital (owl eye, eye mask, raccoon eye) ② scalp ③ extremities



Late onset LE

- In the elderly (>50 years) characterized by :
  - ↑ incidence of neurological & pul. Manifestations.
  - Phtotsensetivity
  - +ve Anti -Ro-abs



Late onset LE

- In the elderly (>50 years) characterized by :
  - ↑ incidence of neurological & pul. Manifestations.
  - Phtotsensetivity
  - +ve Anti -Ro-abs

Neonatal L.E

Q:- Neonatal L.E.

* it occurs Mainly in Female infants of Mothers who have or will develop Connective tissue disease.
* ↑ prevelance of HLA-B8, DR3 in Mothers of Neonates with Neonatal LE.
* Anti- Ro antibodies (Serological Markers) are present in both The Mother & infants, and disappear by 4-6 months of age from infant
* Clinically:- The infant will develop :-

Cutaneouse Manifestations

(1) Subacute CLE-like Lesions in The form of Scaly annular polycyclic erythematouse Lesions. That develop within The 1st 2 months of Life. & improves in 4-6 months ;

Site :- (1) Face :- periorbital (racoon eye) (owel-eye) (eye-mask)

(2) Scalp

(3) extermites.

Healing Lesions resolve without scarring.

(2) Photosenstivity (very common).

Extra-Cutaneouse Manifestation

(1) Complete Congenital heart disease block (Permenant; * may occur in absence of Skin disease).

(2) Hepatobiliary disease

(3) Transient Thrombocytopenia

→ Both → may be present at birth → or develop with few months

* Investigations

Infant should be evaluated for internal involvement:-

(1) Cardic (electrocardiogram)

(2) Hematological (CBC)

(3) Hepatic (Liver Functions test)

→ when indicated

* Treatement:-

(1) Cutaneouse lesions → Mild, require no treatement (Sun avoidance, Low potent Topical Ster)

(2) Cardic : pace maker always required.

(3) hepatic & hematological → reversible (Self limited)

Anti-phospholipid Syndrome

* **Definition:** Anti-phospholipid Syndrome → Multiple System disorder characterized by:
  - elevated (APAs)
  - arterial / venous Thrombosis
  - Thrombocytopenia
  - recurrent Spontaneous abortion.

(APAs) → heterogeneous group of Circulating autoantibodies directed against.
- ve negatively charged phospholipid Compound

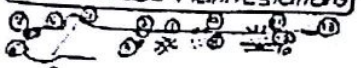
→ include: a) Anti-Cardiolipin
b) Lupus-anticoagulant.
c) Anti B_2 glycoprotein I antibodies
(on 2 or more occasions at least 12 weeks apart)
These antibodies not bind to phospholipids themselves but bind to proteins bound to phospholipid. e.g cardiolipin.

* **Types** → (1) Primary APL antibody Syndrome
(2) Secondry APL antibody Syndrome → associated with Lupus, Lupus like Syndromes, other diseases
all women with SLE and repeated abortion should be screened for Lupus anticoagulant.

* **Pathogenesis**
  - The Mechanism of Thrombosis is not yet defined
  - May be:
    1. Activation of platelets → by interaction with platelet Membrane phospholipid → activation of coagulation
    2. Interference with anti-Thrombotic Mechanisms eg
       - protein S and C pathways & anti-Thrombin III activity
       - release of endothelial prostacyclin / plasminogen activator
       - Activation of preKallekrin → Kallekrien

* **Clinical Features:**

Cutaneous Manifestations — Q: Cutaneous Manifestations of Anti-phospholipid Syndrome.



1. Livedo reticularis
2. Ulceration
3. Necrosis
4. Raynaud's phenomena.
5. Acrocyanosis
6. Digital ischemia / gangrene.
7. Blue toe.
8. Purpuric / cyanotic macules
9. Nodules
10. Thrombophlebitis
11. Hemorrhage
12. Splinter Hemorrhage
13. Porcelain white atrophic scar

Systemic affection
- Many organ/systems involved.
- (1) Deep venous Thrombosis (DVT)
- (2) Pulmonary embolism
- (3) CNS diseases.
  - Arterial occlusion → brain ischemia
  - repeated ischemic attacks.
- (4) repeated Spontaneous abortion.

Catastrophic anti-phospholipid Syndrome
- Multi-organ failure (renal involvement, Acute resp. distress syndrome)
- perciptated by → (1) Surgical procedure
  (2) infection
  (3) discontinuation of anti-Coagulant Therapy
  (4) Drugs (Captopril - Oral Contraceptive pills)

* **Diagnostic Criteria:** «Diagnosis requires at least (1) Clinical & (1) Laboratory criterion.

Clinical Criteria

Vascular Thrombosis
- or more clinical episode of arterial / venous / small vessel Thrombosis

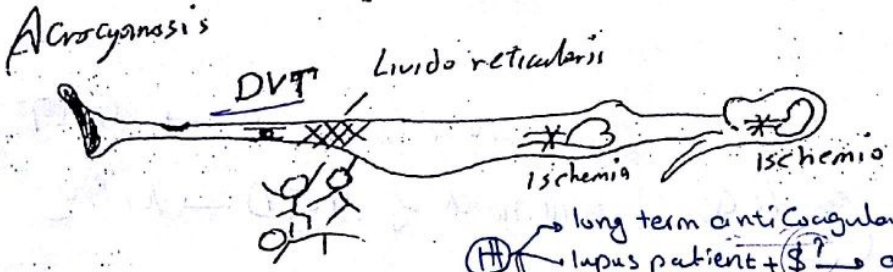
Complications of pregnancy
- or more → unexplained death → of Morphologically Normal fetus → at or after 10 wks of pregnancy
- or more → Premature birth → of Morphologically Normal fetus → at or after 34 wks of gestation.
- or more → unexplained → consecutive Spontaneous abortion. → before 10 wks of pregnancy

Laboratory criteria
1. Anti-Cardiolipin (IgM-IgG) Moderate or high level
2. Lupus anticoagulant Abs
3. anti B_2 glycoprotein I antibodies (IgM, IgG) >99%.

on 2 or more occasions at least 12 weeks apart.

Antiphospholipid antibody Syndrome

- It is a hypercoagulable condition that leads to both venous & arterial occlusions.
- The main serological marker is the detection of circulating antibodies directed against phospholipid (Antiphospholipid antibodies). Cell wall من كل
- Antiphospholipid antibodies present in the form of lupus anticoagulant or anticardiolipin antibodies.
- Antiphospholipid antibodies have been detected by ELISA in 20-50% of cases of SLE & other C.T diseases. Behcet syndrome, lymphoma, $ & AIDS. Nonspecific Ab
- **Clinically :**
  - Venous occlusion → DVT or axillary vein thrombosis.
  - Arterial occlusion → brain ischaemia or transient ischemic attacks.
  - Repeated spontaneous abortions.
  - Other features of the syndrome e.g. livido reticularis. Acrocyanosis, Leg ulcers & thrombocytopenia.



- **Treatment :**
  - Systemic steroid : 40-60mg prednisone + (in SLE disease)
  - Asprin 75mg/d. Usually result in successful pregnancy.

long term anticoagulant (Heparin, warfarin)
lupus patient + $? → anti malarial.
systemic steroid
plasmapheresis + IVIg

N.B. : All women with SLE & repeated abortion should be screened for the lupus anticoagulant.

Lupus anticoagulant antibody

Mixed Connective tissue Disease (~~MCTD~~) Management of MCTD

Def : MCTDs refers to → ① Combination of features similar to those of SLE, SS, DM/PM and/or RA
② associated with auto antibodies to U_1-RNP

Overlap Syndrome → Two or more auto immune disease occur in the same individual simultaneously
eg : SLE, SS, DM/PM, RA in varios combination

- **Epidemiology :** Age : all age groups
  Sex : female : male 16 : 1
- **pathogenesis** (pathophysiology of MCTD) ← genetic, immunol, inflam ← T & B, immunecomplex

Genetic Susceptibility
HLA-DR_2 , HLA-DR_4

Immunological dysregulation
- There is both T and B cell response with less immune complex formation.
  ⓐ B cell response : ↑ high titre of anti U_1RNP
  ⓑ T cell response : reactive T cells are found in peripheral blood.
  ⓒ Immune Complexes : relatively low level of immune complexes found in the circulation (compared to SLE)

Inflammatory response
- proliferative **Vasculopathy** in large, medium and small vessels with less inflammatory infiltrate.
- ++ Synthesis of Type III Collagen → result in abnormal Type I - Type III ratio.

- **Clinical Features :** (Cutaneouse Manifestations of MCTD) (Major diagnostic Criteria of MCTD)
→ **Most**, if not **all**, of the major organ systems may be involved during the course of MCTD.

① Fever.
② Skin & mucose membrane : Raynaud's phenomena (75% - 100%) ✓ Most common skin change
- Malar rash, generalized erythematous rash, pigmentation / de-pigmentation.

③ Vasoular involvement - Raynaud's phenomena
④ Muscles : Myalgia - Myositis (in 30 - 50% of patients) → Similar to DM/PM.
⑤ Joints : arthritis with deformitico (in 60% of patients) → Similar to RA.
⑥ GIT : → Disordered Motility in upper GIT ✓✓ Commonest problem
↳ Symptoms vary from heat burn, Malabsorption, dysphagia diarrhea.
⑦ Heart → All three layers may be involved, Pericarditis ✓ Commonest manif. of Cardic involvement.
⑧ Lung → Major cause of death in MCTD is pulmonary hypertension
↳ pleuro-pulmonary involvement → pleural effusion, pleuritic pain, PTH, Aspiration pneumonia, ILD
⑨ Kidney XXXX → absence of Severe renal disease is **Hallmark** of MCTD.
⑩ Neurological involvement → XXXX Lack of CNS involvement.
↳ Neurological manif 20% of patients → FN, aseptic meningitis.

- **Diagnostic Criteria**

(A) Serological Criteria
Anti U_1 RNP → B cell
at hemagglutination
≥ 1 : 1600

(B) Clinical Criteria
(1) Raynaud's phenomena.
(2) Swollen hands (Edema)
(3) Acrosclerosis.
(4) Synovitis
(5) Myositis

MCTD is present if :
(A) is associated with (3) or more clinical criteria (one of them is **Synovitis / Myositis**)

Q: Serology of MCTD.

Serology:

① Anti U1 RNP antibodies — highly characteristic feature of MCTD
② ANA +ve — 100% in patients, high titre, coarse Speckled pattern
③ RF +ve — 50–70% of patients
④ APL Abs occur less common than in those with SLE
⑤ Absence of XXX anti-Sm, anti-ds DNA Abs (differentiating MCTD from SLE)

Others:

⑪ Hypergammaglobulinemia
- ↑ ESR
- +ve Coomb's test
- Anaemia / Leucopenia

* Management of MCTD:- (Management of MCTD).

→ According to the System(s) affected: for example:-

① Mild MCTD → Raynauds ph, Arthritis, Fever
- avoid cold exposure
- NSAIDs
- Low-dose steroids
- Anti-malarial.

② Disease activity like RA
- NSAID
- Low-dose steroids
- anti-malarial.
- Methotrexate or Immuno-Suppressive drugs.

③ SLE-like
- (Mild-Moderate) involvement
  - avoid Sun exposure.
  - Topical steroid.
  - Low dose Steroid
  - anti-malarial.
- severe organ involvement → Moderate to high dose Steroids.
  Cyclophosphamide
  Other immuno Suppressive agents

) Esophegal involvement without upper sphincter involvement
- raise head end of the bed.
- avoid coffe, Smoking.
- Proton-pump inhibitors. (H_1)

PAH (pulmonary arterial hypertension)
- asymptomatic → CCB, ACE inhibitors, UD
- Severe → CCB, ACE inhibitors, Corticosteroids, immuno Suppressi

A/e of DM:-

- unknown
- believed to be immune mediated response triggered by exogenous

① Genetic susceptability:- HLAB8, DR2 DR52

② exogenous :- infections → enteroVirus
Drugs → D. penicillamine
maligrancy → in adult onset DM

③ Immune response:- - associated é other autoimmune disease
- presence of autoantibodies → ANA notspecf
anti Ku ← anti Jo1 anti Mi-2

association → malignancy → paraneoplastic
occur in adult onset DM
é Bronchogic carcinom, Breast Cancer

→ other CT disease
overLap syndrome → CREST SLE MCTD
SS sjogren

→ other autoimmune disease → Graves
Hashimoto
type I DM

D penicillan → DM
SLE
↓
+ve antihistone Ab
→ Cut and systemic c/p of SLE

Dermatomyositis (DM)

It is a systemic autoimmune, inflammatory C.T disease affecting both the skin and muscles.

* **Epidemiology** :

- Age : ↑ 40y juvenile form of DM occur before the age of 10 years
- Sex : female : male = 2 : 1

* **Classification** :

- Polymyositis (PM)
- Dermatomyositis (DM)
- PM or DM
- Childhood DM.

* **Etiology** :

- Unknown.
- Int. malignancy e.g breast cancer, bronchogenic carcinoma..
- Autoimmune : several myositis-associated antibodies have
  - . Anti – Jo-1 abs : mostly seen in PM
  - . Anti – Mi-2 abs : in 20% of pt's with DM.
  - . Anti – Ku abs : marker for sclerodermatomyositis.

* **Clinically** :

(I) Cutaneous features : are often pruritic → d.d. of LS → non pruritic

1. Periorbital heliotrope violaceous erythema usually associated with some degree of edema of eyelids.
2. Gottron's papule :

   Flat topped, violaceous papules over the dorsal surface of interphalangeal joints of the hands.
3. Gottron's sign :

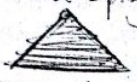
   Violaceous erythema overlying the dorsal aspect of hands.

tissue

2 Gyp C

4. Periungual erythema & telangiectasia + ragged cuticle. (Somite sign) not specific

5. Poikiloderma. ⇒ ① atrophy ② mottling hypo/hyperpigmentation ③ Shawl sign → distribution of poikiloder on shoulder, arm, back



d.d red → violaceous in LE

6. Calcinosis cutis : ترسب كالسيوم في الجلد

Calcification in S.C tissues → more in Jeuvenile DM

7. Photosensetivity, Urticaria, hyperpigmentation in later stage & erythema multiform like lesions, acquired ichthyosis

(II) Skeletal muscle affection : (gradually, progressive)

- Progressive symmetric weakness & later atrophy of the proximal muscles of the extremities → difficulty in rising from sitting without using arms.
- Muscle atrophy & muscle tenderness may be evident on palpation.
- Dysphagia is seen in 50% of patients due to esophageal muscle involvement. (esophageal dysmotility) he can not swallow without drinking water
- Involvement of the diaphragm may induce respiratory failure.

- myocitis → progressive muscle weakness

CpK ↑ Creatine phosphokinase (lab)

ischemic pain

- Cardiac affection → arrhythmia, myocarditis → bad prognostic sign.

(III) Systemic manifestation : Rare in contrast to SLE malaise

N.B. :

- Pregnancy exacerbates DM in 50% of cases with increased incidence of fetal loss. DM can start in pregnancy.

DD LE → pregnancy have no role in fetal loss, common in cardiolipin

★ amyopathic ...

- classic cut. manifestation of DM ēout muscle affection
-

★ sclero dermatomyositis

↓ scleroderma Limited to Face, hands	↓ DM or PM	Rayaund's non erosive arthritis esophageal, Lung affect	+ve RF +ve DM-SCL Abs

★ anti-synthase syndrome

- anti synthetase Ab +ve
- anti Jo-1 +ve

Rayn
non erosive arthritis
interstitial lung dis
mechanic hand

fever

Diagnosis of DM:-

[عينة جلد عينة دم عينة بول]

- Biopsy
  - poikilodermic site → LE-like H/p
  - Gottron papule → acanthosis + Lichenoid infilterate
- serum → ESR ↑ creatine phosphokinase ↑ LDH ↑ lactate dehydrogenase
  ANA Anti Jo1 anti Mi2
- urine → Creatine

[رسم عضلات عينة عضلات أشعة عضلات]

EMG electromyography → abnormal > 90% ē DM

muscle biopsy
- atrophy, necrosis, Lymphocyte infil
- Not from deltoid that affected very late
- From triceps muscle
- done in Case of absence of classic cut. lesion

Muscle imaging → Diagnosis

Diagnostic criteria For DM/PM.

1. proximal symmetric progressive muscle weakness
2. Electromyogram of amyopathy
3. Muscle biopsy → evidence of inflamatory myopathy.
4. Typical cut. lesion
5. elevated CPK, LDH, SGOT, SGPT

(Possible) 2 present

(probable) 3 present

(sure) 4 present

- Childhood DM (juvenile), characterized by :
  - Malignancy is rare.
  - Much more sever than in adult.
  - Calcification occurs more frequent (+ small vessel vasculitis)
  - Child recovers without any residual disability.
  - Recurrences are rare.
  - Low grade fever.

Diagnosis :

D.D ~~of other~~ Causes of poikiloderm
- LE
- Psoriasis
- CTCL
- photodrug eruption

1. History and clinical examinations.
2. Laboratory investigations :
   a. Creatine kinase (CPK) : Elevated in acute active phase.
   b. ESR : Elevated
   c. Urine : Elevated urine creatin kinase.
   d. Electromyography : Abnormal.
   e. Muscle biopsy : Muscle atrophy a fibrosis.
   f. +ve anti-Jo-1 antibody.

(III) Histopathology : LE

Skin :

Falttening of epidermis (atrophy)

Hydropic degeneration of basal cell layer

Upper dermal edema

Scattered inf. infiltrate

Fibrinoid deposites in upper dermis, and around upper dermal B.V.

Muscle :

Muscle necrosis

* Treatement of Dermatomyositis :-

Management plan :- A patient with characteristic cutaneourse eruption of DM should be submitted to:

1. Skin biopsy :- to Confirm the diagnosis of DM
2. Search For Muscle disease (Myositis) → « affect Therapeutic decision »
3. Search For associated systemic disease → « affect Therapeutic decision »
4. Search For Feature of overlap with other AI CTDs.
5. Screening for Occult Malignancy (in adults with DM or amyopathic DM)
6. Start treatement accordingly

prognosis

* Indicators of good prognosis :- – Calcinosis cutis (Juvenille DM)
  – Absence of Muscle affection (Skin-limited disease)
* Indicators of poor prognosis :- – Malignancy
  – Cardic disease
  – pulmonary / GIT affection.
  – Older age / progressive disease.
  – Longer duration of Symptoms before diagnosis
  – Extensive cutaneourse involvement of The Trunk.
  – Intiation of Therapy after 24 Months (2y) of Muscle weakness
* Causes of Death in DM :- – Malignancy
  – Cardic Failure.
  – respiratory infection.
  – Malnutrition (Difficulty in swallowing)
  – Side effect of Steroid Therpy

Treatement

Treatement of Cutaneourse disease :-

1) Photoprotection (SunScreen)
2) Topical Corticosteroid / Tacrolimus.
3) Anti-malarial Therapy
4) Immuno-Suppressive :- Low dose weekly Methotrexate
   Mycophenolate Mofitel.
   Dapsone, Thalidomide.
5) IVIg
6) Retinoids
7) Biologic :- TNF-α blockers (influximab - Etanercept)
   Rutiximb.
8) tt of Calcinosis cutis :-
   - Surgical excision
   - Ca channel blockers (diltiazem).
   - ESWL (electric Shock wave Lithotripsy)

Treatement of Muscle disease.

(1) Rest (in acute Stage).
(2) physiotherapy (To prevent deformaties & Contractures)
(3) Systemic Corticosteroids
   Prednisone 1mg/kg/day
(4) Pulse Corticosteroid + Steroid Sparing agents (For Severe Cases)

Methotrexate, Azathioprine, Mycophenolate cyclophosphamide, cyclosporine, IVIg Etanercept, infliximb, plasmapheresis.

* Wong's dermatomyositis *
- Rare DM Subtype
- Characterized by PRP-like lesions (Hyperkeratotic cutaneourse lesions That resemble clinically & Histopathologically PRP in DM patient

Treatment :

1. Complete rest.
2. Prednisone 0.5-1mg/kgm BW/d increased to 1.5mg/kg.
3. Azathioprine, cyclophosphamide or cyclosporine.
4. Methotrexate.
5. Antimalarial. Plaquenil 200mg x 2
6. High-dose of IV immunoglobulin bolus therapy/monthly.
7. Topical steroid & sunscreen (for photosensitivity).
8. Malignancy should be excluded.

Elidel (pimecrolimus)

SJÖGREN'S Syndrome

(Mikulicz's disease)

Def/ autoimmune disease affect → secretory gland

dry eye
dry mouth

This syndrome comprises the triad of :

1. Dryness & atrophy of the conjunctiva and cornea.
2. Dry mouth.
3. Rheumatoid arthritis. Morning stiffness

Associated systemic features :

- Arthralgia.
- Dysphagia.
- Raynud's phenomenon
- Renal affection.

Cutaneous manifestations :
- xerostomia
- urticarial vasculitis
- petechia
- erythema
- purpura

Treatment : Artificial tears + saliva replacement solutions. + immunosuppressive in organ involvement

Lab → ↑ESR, leucopnea RF+ve anti Ro anti La

H&P → Dense lymphocytic infiltrate around salivary gland

Periorbital dermatitis

* **Raynaud's phenomena**

→ Def: Episodic vasospasm of the digital arteries (secondry to cold stimuli) → white, blue, and red discoloration of the fingers.

→ 2 types: primary and secondry

	Primary Raynaud's	Secondry Raynaud's
- Synonyms	• Raynaud's disease.	
- Incidence	• Common	• uncommon.
- Association	• Not associated with underlying disorder	• associated with underlying disorder eg (SSc is one of Commonest)
- Age of onset	• Puberty	>25yrs
- Sex	• ♀:♂ (20:1)	♀:♂ (4:1).
- Frequency of attacks	• <5 per day	≥5-10 per day
- peripitants	• Cold emotional Stress	• Cold.
- Ischemic injuiry - Abnormal capaillorscopy - autoantibodies (ANA, Anti SCL-70 Anticentrome)	Absent	Present

→ Treatement:

1st Line → avoid Cold. & Tobacco products.

2nd Line → (1) VD → CCB (nifedipine)
- Ang II receptor blocker. (losartan).
- PDE5 Type 5 inhibitor (sildinafil / tadalafil)

(2) ↓ low dose aspirin, Pentoxyphiline

(3) IV PGE1

(4) Nerve block, sympathectomie.

(5) Topical Preparations (ineffective)

---

* **Esinophilic Fascitis (Shulman's Syndrome)**

→ Sclero-derma like Syndrome. ; Deep Fascitis with esinophilia.

→ H/O of Trauma (30%)

C/P **Initially** → Oedema & pain of involved extremities

↓

quickly progress to fibrosis & dimpled appearance.

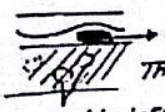
* Condition affect extremities, in Symmetric Faschion.

* **Groove Sign** → Linear depressions where viens appear to been Sunken within indurated skin.

Lab ↑ESR - Hypegammaglobulinemia - peripheral esinophilia

Associated → pancytopenia (Anaemia / Thrombocytopenia) + Hematologic Malignancy (Myeloproliferative disorder).

HIP



→ Dermal fibrosis

Thickening of deep Fascia (10-50 times the normal width)

patchy infilterate (lymphocytes - plasma cells) in Fascia

Treatement

* Prompt Treatement (oral Corticosteroids) → to preserve Mobility & Function

* if Inadequate → Methotrexate / cyclosporine
- Hydroxychloroquine.
- PUVA - UVA,

→ used alone or Combined to prednisone

Scleroderma

It is a multisystem disease of unknown cause. It may be localized to the skin (morphea) or involve the skin and internal organs.

Scleroderma

Localized (morphea)

Systemic sclerosis

- ***Limited cutaneous systemic sclerosis***
- ***Diffuse cutaneous systemic sclerosis***

	Limited CSS	Diffuse CSS
• Onset	Gradual	Abrupt
• Skin sclerosis	Face, forearm & hands.	Hands and Trunk
• Raynoud's phenomenon	Long history	Within one year of onset of skin changes
• Systemic affection	Late onset of pul. Hypertension	Early onset of lungs heart stomach & renal diseases
• Nail fold capillary	Dilatation	Dilatation & destruction
• Auto antibody	+ve anticentromer AB	+ve SCL 70 AB -ve anticentromere AB
• Prognosis	Good	Poor

Localized Scleroderma (Morphea)

* **Definition** :

It is a localized cutaneous sclerosis characterized by early violaceous, later ivory-white plaques, which may be solitary, linear, generalized & rarely accompaind by atrophy of underlying structures. morphea is differentiated from systemic sclerosis by absence of sclerodactly, Raynaund's phenomenon, Nail fold capillary change, organ involvement

* **Epidemiology** :

Female : Male = 3 : 1

Age : 20 – 40 years.

* **Etiology** :

Unknown, it may be caused by Borrelia burgdorferi infection.

* **Clinical varieties** : systemic C/P → not rare most common arthalgia, CNS Affection

1) Plaque (circumscribed) morphea: most common presentation in adult

- Site : Trunk, Limbs, face & genetalia.
- C.P : Single or multiple plaques, indurated in consistency, Ivory white in color with violecious lilac border.

- head é residual pigmentation

2) Pansclerotic morphea (morphea profunda) :

- Site : there is involvement of dermis fat, muscle and bone pansclerotic morphea is usually generalized occurring on the trunk extremities, face and scalp with sparing of finger tip and toes.

3) Segmental morphea : (UA1)

- Site : Face.
- Hemiatrophy on one side of the face.

4) Guttate morphea :

- Site : Trunk.
- C.P. : Small whitish atrophic macules resembles lichen sclerosis et atrophicus but doesn't show hyperkeratosis or follicular bluggings.

5) Generalized morphea :

- It occurs initially on the trunk. Extensive involvement → restricted respiration.
- There is no systemic involvement.
- Bullus lesions may be seen !! (the only tipe of sclroder

6) Linear morphea : (en coup de sabre)

- Sites : most common presentation in children

  * It usually occur on extremities → contracture of joints.
  * Face : En coup de sabre : Linear depressed groove on the frontoparietal region, scalp involvement → alopecia.
  * Nail dystrophy may occur.

7) Bullous morphea

8) as a Component of overlap syndrome MCTD sclerodermatomyositis

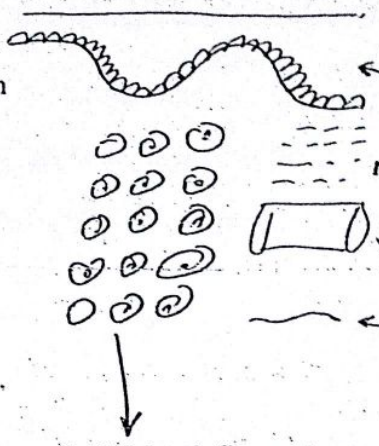
Diagnosis :

1. History & examination.
2. Histopathology :

Early

(1) Edema
swelling degeneration
of collagen fibrils

Early inflamatory stage :-
- lymphocytic inf. infm in Lower dermis, Sc fat
- Large area are replaced by newly formed collagen
- thick trabeculae of sc fat.
- ↑ mast cells

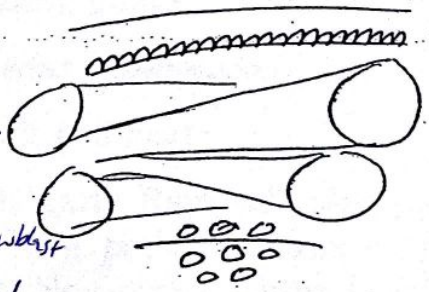


- **Epidermis** : Normal or atrophic with loss of rete-ridges.
- **Dermis** :
  1. Initially : edematous with swelling and degeneration of collagen fibrils

2. Slight inflammatory infiltrate :
- Perivascular or diffuse.
- lymphocyte, macrophage or plasma cells.

Later

Late sclerotic :-
- infiltrate disappear.
- Collagen consist of thick closely packed hyalinized bundle & fibroblast
- atrophic eccrine gland.



- **Epidermis** : Atrophic
- **Dermis** :
  - Thickened with few fibroplast & dense collagen.
  - Inflammatory cells at dermal/subacutes junction.

Treatment :
1. Intra lesional injection of triamicinolone.
2. Penicillamine (Antifibrotic agent).
3. PUVA.

Systemic Scleroderma (Systemic sclerosis)

more in 4th decade ♀ : ♂ 3 : 1

Scleroderma is a multisystem disorder characterized by inflammatory, vascular and sclerotic changes of the skin and a variety of internal organs especially the lungs, heart and GIT.

* Etiology :

- Unknown.
- Autoimmune.
- Vascular changes.

* Clinical features :

[I] Limited cutenous systemic sclerosis : (acrosclerosis) CREST

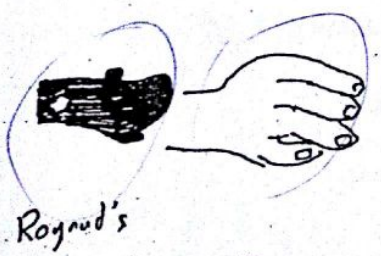
- It starts with Raynoud's phenomenon many years before any skin changes.
- **Clinically :**

A. ***Symptoms*** : (1) Raynaud's phenomenon with digit pain, coldness & tingling.

B. ***Cutaneous examination*** :

1. Hands and Feet :

R ▪ Early Raynoud's phenomenon with color changes e.g. pallor, cyanosis & rubor.
E ▪ Non-pitting edema of the ~~nads~~ hands & feet → can't be fully extended.
U ▪ Painful ulcerations at fingertips & knuckles may occur
C ▪ Cutaneous calcifications of fingers may be seen.
T ▪ Periungual telangectasia.



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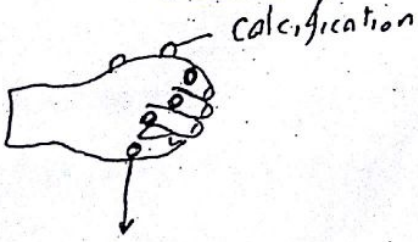
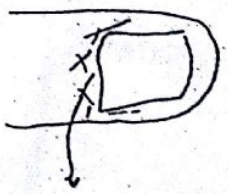


Ulceration



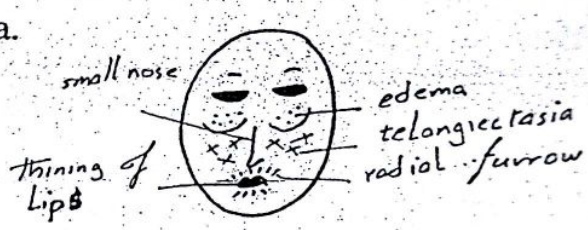
periungal telangectasia

. dissimenated telangectasia.

- Raynaud

1) Hand and feet ← Raynaud, edema, ulceration – calcification, telangiectasia

2. Calcinosis cutis :
   - Witish papules occurs over bony prominences. It may ulcerate and extrude white paste.
3. Face :
   - Early: Periorbital edema.
   - Later : edema & fibrosis result in loss of normal facial lines, thining of lips, microstomia, radial perioral furrowing & small sharp nose + fascial telangiectasia.



4. Hyper & hypopigmentation.
5. CREST syndrome :consist of
   - Calcinosis.
   - Raynaud's phenomenon.
   - Esophageal dysmotility.
   - Sclerodactyly.
   - Telangectasia.

C. ***Systemic manifestations*** :

Esophageal symptoms, pulmonary hypertension …

[II] Diffuse cutaneous scleroderma (DCSS)

- Skin sclerosis involve skin distal
- No telangectasia.
- short interval <1year between Raynaud and skin changes

A. ***Symptoms*** :

- Early involvement of organs → e.g. GIT → anorexia & weight loss , lung → dry cough …

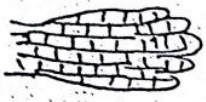
Diffuse DCSS

a- Early involvement of organs → GIT, renal, ... lung

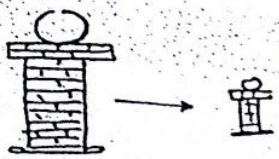
B. ***Cutaneous examination*** :

- Raynaud's phenomenon develop later (after 1 year).
- Skin lesions :

  - Hand changes start first. skin become edematous.
  - There is telangiectasia and abnormal nailfold capillaries.



  - Diffuse swelling & stiffness of fingers occur.
  - Stiffness may involve most of the body in sever cases → later the skin becomes atrophic.



C. ***Systemic Manifestation*** :

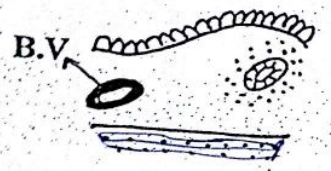
- Musculoskeletal manifestations :
  - Pain & stiffness of fingers & knees.
  - Polyarthritis …
- Gastrointestinal manifestations :
  - Esophageal dysmotility, malabsorptition.
- Respiratory manifestations :
  - Lung fibrosis.
- Renal affection.
- Heart affection.
- CNS affection.
- Eye affection.

N.B. : Sometimes systemic manifestations occur without skin involvement (scleroderma sine scleroderma)

Diagnosis :

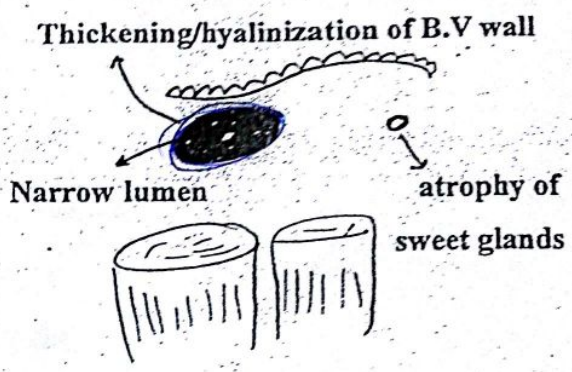
1. *History & examination.*
2. *Histopathology :*

Early



Mild cellular infiltrate around dermal B.V, eccrine gland & S.C tissue

Late



3. *Lab. Findings :*
   - In localized CSS : +ve anticentromere antibody.
   - In diffuse CSS : +ve SCL-70 antibody.
   - Rheumatoid factor : +ve in 30% of cases.
   - ESR : may be +ve.

[III] Radiography :

- Chest x-ray : honey comb lung
- Barium swallow – for impaired asophageal motility.

Diagnostic criteria (American College of Rheumatology)

In 97% certain with ① major or ② minor criteria

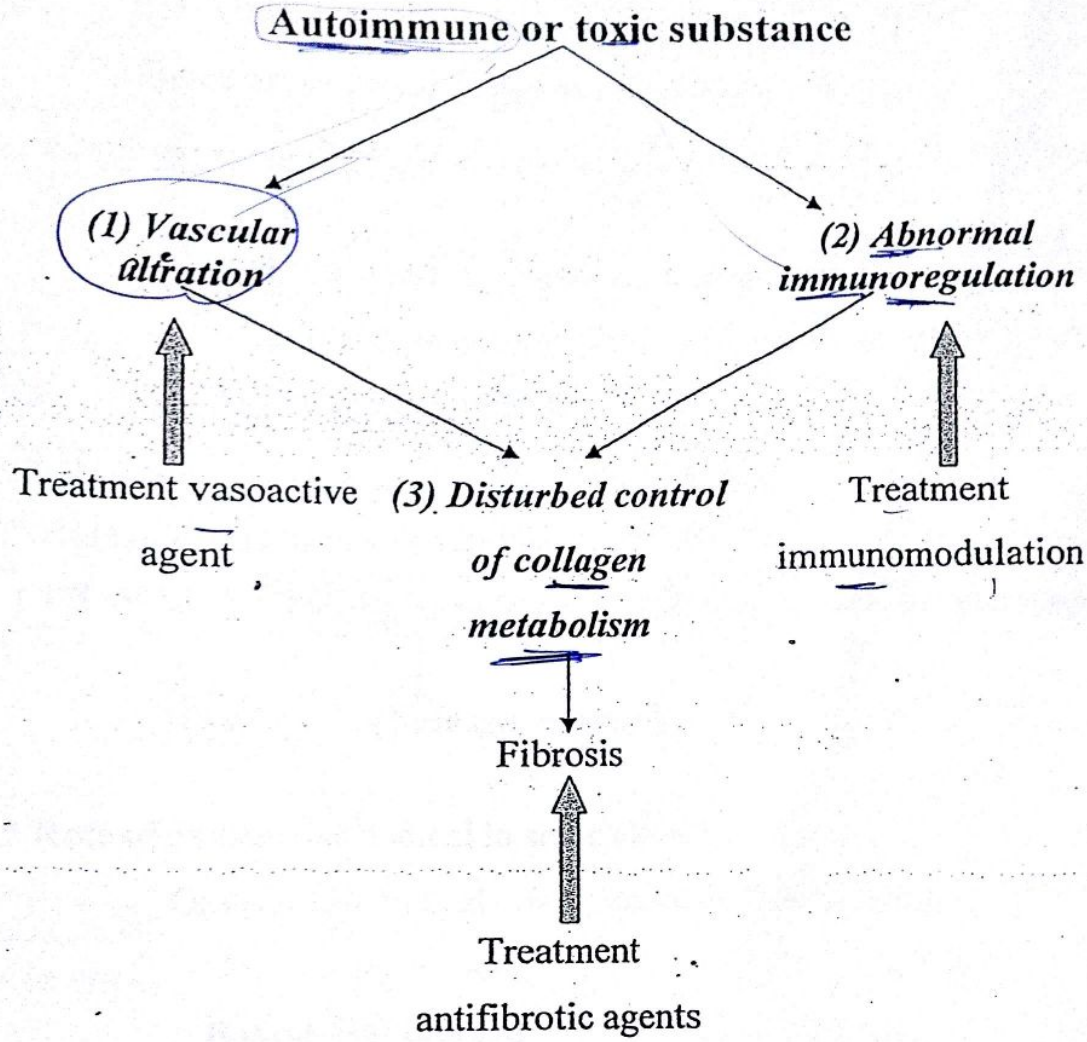
Major

proximal (truncal) sclerosis

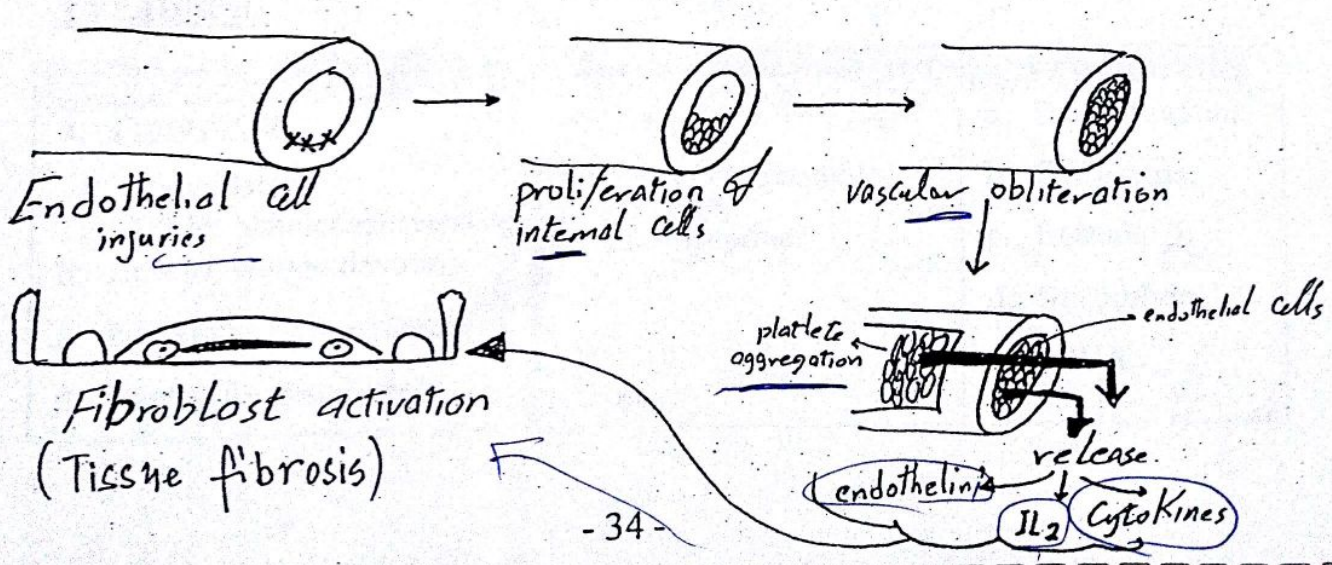
minor

- sclerodactly
- digital pitting scar
- loss of substance of digit finger pad
- Bibasilar pulmonary fibrosis

Pathogenesis :



(1) *Vascular alteration* :



(2) *Abnormal immunoregulation* :

- Humoral immunity → ↑ antinuclear AB.
- ↑ TH cell activity.

(3) *Disturbed control of collagen metabolism* :

Activated fibroblast → ↑ synthesis of collagen type I & III + fibrinonectin + glycosaminoglycans → lower dermal fibrosis + fibrosis in internal organs.

N.B. :

* Role of mast cell in scleroderma :

↑ TH → IL5 → **Mast cell stimulation** → **protease** → **endothelial damage**

Mast cell stimulation → **Histamine** → ↑↑ **collagen synthesis**

* Role of oxygen free radical in scleroderma :

Drugs, pollutions, Dead cells → Oxygen free radical → fibroblast proliferation

Oxygen free radical → Endothelial damage

fibroblast proliferation → Fibrosis

Treatment :

(1) Vaso-active agents	(2) Immunomodulators	(3) Antifibrotics
a. Prostacyclin : - Vasodilator. - Inhibit platelet aggregation b. Low M. weight dextran : c. Nifedipine : vasodilators. d. Captopril : vasodilators	a. Prednisone 5-10 mg/d b. Cyclophosphamide c. Azathioprine	a. D.pencillamins. b. Colchacine. c. Isotretinoin d. Grisofulvin e. PUVA

Pseudoscleroderma

Many diseases or environmental factors can induce sclerodermatous changes e.g. :

1. Genetic :
   - Rothmund – Thomson syndrome.
2. Metabolic :
   - Amyloidosis.
   - Porpheria cutanea tarda.
   - Scleroderma.
   - Scleromyxedema.
3. Paraneoplastic syndromes :
   - Carcinoid syndrome.
4. Graft varsus host disease.
5. C.T. diseases :
   - SLE.
   - Dermatomyocitis.
6. Occupational :
   - Silicosis.
   - Vibration syndrome.

Eosinophilic fasciitis (shulman's syndrome)

It is an inflammatory disorder characterized by subsequent induration of the skin & SC tissues associated with peripheral eosinophilia.

Treatment :

1. Prednisone 40mg/d.
2. Methotrexate.
3. Cyclosporine A.